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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,076	02/20/2002	Paul A. Barstad	252312006002	4811

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 09/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,076	COUTTS ET AL.	
	Examiner	Art Unit	
	David A Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-43* is/are pending in the application.

4a) Of the above claim(s) *33-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-32 and 38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/23/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 28-43 are pending.

Applicant's election without traverse of Group I, (claims 28-32 and 38-43) in the reply filed on filed 6/14/04 is acknowledged.

The election did not state any traverse but merely requested rejoinder of the method claims. It is to be noted that examiner has cited art (e.g. disclosure of anti-idiotypic antibodies) against the product claims under examination that could not have been cited against the method claims. Likewise the examiner has cited references of the vaccine art showing peptides comprising B-cell epitopes; these peptides were known prior to characterization of their T-cell reactivity.

It is thus considered that there has been a sufficient burden upon the examiner to search product claims only. Therefore the examiner has not rejoined method claims.

The disclosure is objected to because of the following informalities: at page 1, in the paragraph amendment on 2/20/02, the current status of application 08/118,053 must be updated.

Appropriate correction is required.

Also at page 24, line 7 the examiner counts 8 residues in peptide # 1; applicant then recites "7 mer". Does applicant intend –8 mer--?

A like consideration applies to the length of each "mer" recited at page 24, lines 10, 13, 16, and 19.

Claims 28-32 and 38-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 28, it is not clear whom or what "an individual" is; any "immunogen" as recited at line 1 is only an "immunogen" in certain "individuals". For example, mouse IgG is an "immunogen" in a human "individual" but not in a mouse "individual" of the same strain. In the claim it is not clear whether the "T-cells" of line 3 are from an "individual" who would mount an immune response to the "T-cell dependent immunogen" of line 1, or are from any individual.

Claim 38 recites no "individual" but a like problem arises. It is not clear as to whom or what is the source of the T-cells that would be used to measure the "T-cell stimulation index.

Applicant could overcome by inserting limits of claims 30 and 41 into claims 28 and 38, respectively. In claim 41, "The individual" lacks antecedent basis.

Claims 31-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 31 and 42 are rejected as containing new matter because a generic "buffer" is not supported by the specific recitation of "0.1m sodium borate buffer, pH 9.0" at page 13, lines 26-27.

Claims 32 and 43 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial asserted utility or a well-established utility.

While applicant has described complexes of the immunogen analogs and antibodies as being formed in immunoassays, he has not disclosed a use for the complexes per se. These assay are disclosed (page 8, lines 29+) as being conducted for the purpose of identifying useful immunogen analogs, not for obtaining the complexes. Further the title, abstract, technical Field, Disclosure of the invention, and taught therapeutic utilities (page 12, line 4+) teach nothing about the use of analogue – antibody complexes, nor of any compositions containing such complexes

Claims 32 and 43 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 28-29, 31-32, 38-40 and 42-43 are rejected under 35 U.S.C. 102((a) or (e)) as being anticipated by Tanihara et al (4,925,787).

Tanihara et al disclose an anti-idiotypic (anti-Id) monoclonal antibody that is consistent with the immunogen analog defined in instant claim 28. In this case the "immunogen" is considered to be the nicotinic acetyl choline receptor (AChR), disclosed at col. 1, lines 11-60. As for any protein, this would inherently be a "T-cell dependent immunogen".

Tanihara et al disclose a human monoclonal antibody of the IgGI isotope, which specifically binds the AChR. This antibody mediates the pathology of the autoimmune disease myasthenia gravis, by virtue of specifically binding to the AChR immunogen, as recited in instant claim 30. See Tanihara et al at col. 1, lines 11-20.

Tanihara et al employ this human monoclonal antibody against AChR as an immunogen, in order to produce and anti-ID antibody thereto. See col. 2, lines 23-59, for example.

The anti-ID antibody of Tanihara et al properly anticipates the claimed analogue because: 1) the anti-Id antibody "binds specifically to an antibody (i.e. the anti-AChR antibody) to which the immunogen (i.e. the AChR) binds specifically" as required by claim 28. 2) The anti-Id antibody comprises "an epitope" within its binding site by which binds to the anti-AChR antibody. 3) The anti-Id antibody serves as an immunogen analogue by virtue of the fact that its binding region mimmicks the epitope(s) of AChR which are bound by the anti-AChR auto antibodies of the individual. See for example, col. 2, lines 60-64; col. 6, line 48 – col. 7, line 6. 4) The anti-Id antibody of Tanihara et al "lacks T-cell epitopes capable of activating T-cells in an individual" (at least for the case wherein the "individual" is the mouse used to produce the anti-Id antibody, the mouse

would not have T-cells reactive to any significant degree with its own produced antibodies). Claim 28 does not stipulate who the "individual" is. 5) The anti-Id antibody, like any antibody, is polypeptide in nature. Thus "the analog is a polypeptide". 6) Tanihara et al purify the anti-Id antibody. See col. 6 lines 35-47.

Thus all features of claim 28 are shown. Claims 38-39 is included, since the mouse that produced the anti-Id antibody would show a baseline T-cell stimulation index against its own produced antibody.

Regarding the "functional group for coupling to a carrier" in claims 29 and 40, this is a recitation of intended use, as far as the "coupling to a carrier" is concerned. Tanihara et al disclose compling or conjugation of the disclosed anti-Id antibodies to labels (col. 7, lines 1-5) for immunoassays, or to insoluble carriers (col. 7, line 6-65) for immunoadsorption procedures. Whether one is coupling to a non-immunogenic carrier (as intended instantly) or to a label, or to an insoluble carrier (as in the reference) makes no difference; the same kind of functional group" could be used to couple to any of these.

Regarding claims 31 and 42 Tanihara teach providing the anti-Id antibody in PBS, which is a "buffer" (col. 18, lines 13-15).

With respect to claims 32 and 43, a complex of the anti-Id antibody anti-AChR auto antibody would inherently be formed in any immunoassay or immunoadsorption method disclosed at col. 6, line 48- col. 7, lines 66; see especially col. 7 at lines 59-61 teaching formation of "an immune complex".

As stated supra, this rejection depends upon interpreting the "individual" of claims 28 and 38 as being the mouse that produced the anti-Id antibody. The individual" recited in dependent claims 30 and 41 could not be this mouse. These claims are thus not rejected over Tanihara et al.

Claims 28-29, 31-32, 38-40 and 42-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Milich et al (4,599,231).

Milich et al show polypeptides of Hepatitis B virus surface antigen (H Bs Ag) that comprise a B-cell determinant (epitope). See col. 6, lines 3-53. See also example IV at col. 12, line 44 – col. 14, line 29. Note, therein, Table 1 showing that polypeptides P. 73, P72 and P 49 have B-cell determinants/epitopes. These polypeptides induce minimal T-cell proliferation. See Fig. 3; see col. 15, lines 60-62; col. 16, lines 14-17. Since the intact HBs Ag polypeptide has both B-cell and T-cell epitope (see col. 6, lines 23-27 and 54-58), the polypeptides of Milich et al that contain only B-cell determinants are consistent with the analogue of claim 28.

Claims 38-39 are also rejected. The extremely low responses shown in Fig. 3, for peptides P73, P72 and P49 (Fig. 3a) and for p49 (Fig 3b) are taken to be consistent with the recited stimulation index of each claim.

Claims 29 and 40 are rejected because when the peptides of Milich et al are coupled to a carrier, such as KLH (col. 12, line 62), a "functional group for coupling" is inherently necessary.

Claims 31 and 42 are rejected because, when Milich et al synthesize the peptides and resuspend these in culture media for the T-cell proliferation assays, they

are resuspending in a medium, which includes a buffer such as HEPES. See col. 14, lines 30-60.

Claims 32 and 43 are included because complexes of the B-cell epitope containing peptides and antibodies thereto are formed in the immunoassays used to generate the data shown in Table 1.

Claims 28-29, 31-32, 38-40 and 42-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Good et al (4,886,782).

Good et al show the (NANP)n polypeptide, which is a subsequence of the malaria circumsparozite (CS) protein. This (NANP)n polypeptide contains B epitopes but does not contain T-cell stimulating epitopes for mouse strains other than those of the I-A. sup. b genotype. See col. 1, lines 38-59. Since the CS protein has both this B-cell epitope and a T-cell epitope (identified by Good et al as the Th2R sequence). The (NANP)n polypeptide of Good et al has all features of the instant immunogen analog of claim 28.

Claims 38-39 are rejected since a polypeptide that is non-stimulating would be expected to have the recited stimulation index in each case.

Claims 29 and 40 are rejected, since Good et al disclose a derivative of (NANP)n prepared for coupling to a T-cell epitope containing peptide. See col. 4, lines 13-30.

Claims 32 and 43 are included because assays for antibodies binding to the (NANP)n peptide would have formed complexes of the antibody and peptide. See col. 4, lines 36-37 and col. 6, lines 29-43.

Likewise claims 31 and 42 are included because, during the above noted assays the peptide episted in wells containing samples diluted in phosphate buffered saline (col. 6, line 34).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 28 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,060,056. Although the conflicting claims are not identical, they are not patentably distinct from each other because it is considered in the public interest to require a disclaimer to assure common ownership.

Firstly, it is noted that the instant claims, drawn to polypeptide analogues, claim a precurser compound for the synthesis of the conjugates claimed in Pat. No. 6,060,056. It is noted that the instant claims may be considered as drawn to the element A (analogue) while the issued claims may be considered as drawn to A incorporated into the combination A + L + P, in which L is a conjugating linker and P is a platform molecule. Since applicant could have earlier claimed A alone, and since claiming A with

"comprising" encompasses claiming the conjugate, the requirement for a disclaimer is considered proper.

It is to be noted that the relationship between the instant and patented claims is like that of In re Borah 148 USPQ 213 and of General Foods Corp. 23 USPQ2d 1839. In both cases the pending claims recited less than the total number of elements recited in the issued claim. In each case the office was found in error to require a disclaimer for the broader claims reciting less than the issued claims. The Office presently considers the requirement proper because the instant fact situation does not exactly parallel Borah and General Foods. In those causes, the patented claims arose from a second filed application, which was disclosed as an improvement over a first filed application, which disclosed a broader invention for which the claims were still pending. Instantly, however, there was no second filed application disclosing an improvement of the invention of an earlier filed application. In Pat "056 applicant chose to go for the more narrow claims reciting the combination A+L+P. Though he could have claimed A alone, he never even presented such claims.

On attached form 1449, lined out references were not available in this or any other application of its lineage.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Saunders whose telephone number is (571) 272-0849. The examiner can normally be reached on Monday to Thursday from 8 AM to 5:30 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Saunders/LR
September 2, 2004

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